

Anti-VEGF Therapy and Neovascular Glaucoma

Intravitreal injections improve visual outcomes, but the careful monitoring of patients after treatment is necessary.

BY PAUL HARASYMOWYCZ, MD, MSc



The following is not an unusual scenario: your busy glaucoma practice is brought to a halt when the emergency add-on patient arrives with severely elevated IOP and new-onset neovascularization of the anterior segment. In

years past, glaucoma surgery on these patients was often complicated by bleeding that led to hyphema, occluded tube shunts, and the eventual failure of filtering surgery. The emergence of antivascular endothelial growth factor (anti-VEGF) therapy has changed the landscape of managing neovascular glaucoma (NVG). This month's "Peer Review" column discusses recent research on the use of anti-VEGF agents for the treatment of NVG.

—Barbara Smit, MD, PhD, section editor

The identification of VEGF and the pathophysiologic role it plays in neovascular age-related macular degeneration¹ and vascular occlusive diseases of the eye² has revolutionized the therapeutic management of the latter diseases and, more importantly, has improved visual outcomes. Although generally safe, intravitreal injections of anti-VEGF monoclonal antibodies can rarely result in cataract formation, retinal detachment, vitreous hemorrhage, systemic vascular occlusions,¹ endophthalmitis,³ and sustained elevations of IOP.^{4,5} Particularly in patients with glaucoma or glaucoma suspects, the IOP should be measured immediately after an injection is given and monitored in the postinjection period. Over the past few years, researchers have increasingly focused on anti-VEGF therapy for NVG, the subject of this article.

CLINICAL RESULTS

Several studies as well as extensive clinical experience have demonstrated a rapid regression of anterior segment neovascularization following the injection of anti-VEGF agents. When interpreting the results of these studies to apply to patients, glaucoma specialists must remember a continuum. Early in the disease process,

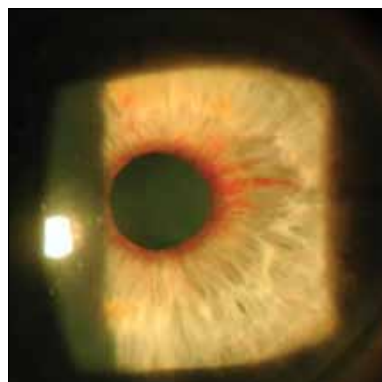


Figure. A patient with neovascularization in the iris.

neovascularization may occur in the iris (NVI) only (Figure), without any new vessels' forming in the angle (NVA); the angle remains open; and the IOP may be normal. As the angle begins to fill with new vessels, and they begin to involute and contract, the

IOP starts to rise. Eventually, the angle will narrow by a "pulling mechanism," ultimately causing complete secondary angle closure and severely elevated IOP.

Wakabayashi et al evaluated the clinical outcomes of intravitreal bevacizumab (IVB; Avastin, Genentech) injection in NVG secondary to ischemic retinal disease and presented results based on this continuum. They found that, when NVI was present without elevated IOP, injections resulted in regression of the neovessels, and the IOP remained normal. Some patients in the NVI-only group required repeat injections. When NVI or NVA was present with open angles and elevated IOP, 40% of patients eventually required surgery to lower their IOP. When NVA and angle closure were present, more than 90% of patients needed glaucoma surgery and IVB to control the IOP.⁶ A randomized controlled study by Yazdani et al showed that, when compared with sham injections, three monthly IVB injections for NVG resulted in a lower IOP and a greater regression of NVI, but the researchers did not observe a difference in rates of surgery or final visual acuity.⁷

Another property of anti-VEGF molecules is their ability to decrease vascular permeability. Ishibashi et al found that, although NVI disappeared clinically 4 to 6 days

after IVB, indocyanine green iris angiography showed the presence of neovessels but demonstrated a significant decrease in dye leakage compared with baseline.⁸ This finding may also explain why patients with intractable NVG who have IVB injections can experience rapid pain relief despite no decrease in IOP.⁹

When glaucoma surgery is planned, the adjunctive use of bevacizumab may be beneficial in NVG. Chen et al demonstrated that, in patients with NVG who underwent trabeculectomy, adjunctive IVB improved final visual acuity and decreased the rates of intra- and postoperative complications, including hyphema.¹⁰ In the trabeculectomy-alone group, the incidence of hyphema was 14% versus 7% in the adjunctive IVB group. Another retrospective study by Ma et al evaluated the adjunctive use of IVB during the implantation of an Ahmed Glaucoma Valve (New World Medical, Inc.) in NVG. The investigators found similar success and complication rates as with those patients who did not receive bevacizumab.¹¹

COMPLICATIONS

The potential complications of anti-VEGF injections have been well described. Higashide et al evaluated the adverse events associated with IVB. Although the investigators found no systemic vascular events, two of 70 patients developed central retinal artery occlusion approximately 3 days after injection. The authors specified that both patients had NVG secondary to ocular ischemic syndrome and recommended caution regarding the use of anti-VEGFs in this clinical situation.¹²

Kotecha et al reported a case of temporary central artery occlusion immediately after IVB that was associated with an IOP of 57 mm Hg and resolved after an anterior chamber paracentesis was performed. They also found that, compared with the angle's configuration at baseline, 6 months after IVB, 35% of patients had progressive angle closure.⁹ This change could be due to recurrent neovascularization or the progressive contraction of the preexisting vascular tissue in the angle. The investigators recommended, therefore, that surgeons regularly perform careful gonioscopy on patients presenting with NVI and NVA, even after anti-VEGF treatment.

Arevalo et al reported tractional retinal detachments as early as 2 weeks after IVB, especially in patients with severe proliferative diabetic retinopathy.¹³ The investigators recommended that surgeons carefully examine the fundus after anti-VEGF injections.

ROUTE, DOSE, AND TIMING OF ANTI-VEGF ADMINISTRATION

The main cause of proliferative anterior segment neovascularization is posterior segment ischemia. Due to the

posterior location—as well as the potential for the vitreous body to serve as a reservoir for the anti-VEGF medication and ensure a prolonged effect—intravitreal injections are a preferred location for injections in NVG. When anatomic landmarks are unclear, or the clinician is more comfortable with anterior segment surgery, intracameral injections are also effective at decreasing NVI and NVA.¹⁴

The timing of injections may be predetermined. In retinal occlusive disease, patients will often receive 3 monthly injections of anti-VEGF agents. In other cases, it may be practical to schedule trabeculectomy or glaucoma tube shunt procedures a few days following intravitreal anti-VEGF injections to decrease hyphema and postoperative macular edema. The ideal dose of injections for NVG is unknown, although Gupta et al found no difference when 1.25 versus 2.5 mg bevacizumab was injected intracamerally during trabeculectomy with mitomycin C for NVG.¹⁵ ■

Section Editor Barbara Smit, MD, PhD, is a glaucoma consultant at the Spokane Eye Clinic and a clinical instructor at the University of Washington School of Medicine in Spokane, Washington. Dr. Smit may be reached at (509) 456-0107; bsmit@spokaneeye.com.

Paul Harasymowycz, MD, MSc, is chief of glaucoma at the University of Montreal and director of the Montreal Glaucoma Institute. Dr. Harasymowycz may be reached at pavloh@igmml.com.



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